REMARKS

Entry of this Amendment is proper under 37 C.F.R. § 1.116 because the Amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration, because the amendments amplify issues previously discussed throughout prosecution; does not present any additional claims; and places the application in better form for an appeal should an appeal be necessary. The Amendment is necessary and was not earlier presented because it is made in response to arguments raised in the final rejection. Entry of the Amendment, reexamination and further and favorable consideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.116, are thus respectfully requested.

As correctly stated in the Official Action, Claims 1, 3-5, and 7-28 are pending in the present application. Claim 24 stands withdrawn from consideration. Claims 11, 13, 14, 18, 20, and 22 stand allowed. Claims 1, 3, 7-10, 12, 15, 17, 19, 21, 23, and 25 stand rejected. Claims 4, 5, and 26-28 stand objected to. Although the Office Action Summary indicates that Claim 28 is allowed, it appears that Claim 28 should be considered rejected as the Office Action later states that Claim 28 stands rejected under 35 U.S.C. § 112.

Applicants note that the Examiner has not acknowledged the entry of the substitute specification filed with the previous Reply & Amendment on May 20, 2002. Applicants respectfully request that the Examiner confirm the entry of this substitute specification.

By the present amendment, the specification has been amended to recite appropriate

labeling of the Figures to correspond with the newly submitted formal drawings for Figures 16 and 18. Accordingly, no new matter has been added.

By the present amendment, Claims 1, 3, 7-9, 24, and 25 have been canceled without prejudice to or disclaimer of the subject matter contained therein. Applicants expressly reserve the right to file a continuation or divisional application on any subject matter canceled in the present application.

Claims 4, 10, 26, and 28 have been amended to incorporate the subject matter of the base claim from which they previously depended. Claims 10, 12, 15, 17, 19, 21, 23, and 28 have been amended as suggested by the Examiner to more precisely define the invention. Accordingly, no new matter has been added.

Drawing Objections

Figures 16 and 18 stand objected to as not labeled correctly. Applicants submit herewith new formal drawings for Figures 16 and 18 labeled as suggested in the Official Action. Withdrawal of this objection is respectfully requested.

Objections to the Specification

The specification stands objected to because the sequences shown in Figures 16 and 18 allegedly do not have an associated SEQ ID NO. Applicants respectfully submit that the Sequence Listing does contain SEQ ID NOs for the sequences of Figures 16 and 18. Moreover, the amended substitute specification filed on May 20, 2002, (which has not been

acknowledged by the Examiner) contains appropriate reference to the SEQ ID NOs for each Figure. Accordingly, withdrawal of this rejection is respectfully requested.

The specification stands further objected to as not having been amended to reflect the labels of Figures 16 and 18. As noted above, the Examiner has not acknowledged the substitute specification filed on May 20, 2002, which included reference to the Figures appropriately. Nevertheless, by the present amendment, Applicants have amended the substitute specification to accurately reflect the labels of Figures 16 and 18 submitted herewith as formal drawings. Accordingly, withdrawal of this rejection is respectfully requested.

Claim Objections

Claims 4 and 5 and 26-28 stand objected to because they depend from rejected claims.

By the present amendment, Claims 4 (from which 5 depends), 26 (from which Claim 27 depends), and Claim 28 have been rewritten in independent form, incorporating the subject matter of the claims from which they previously depended. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 112

Claims 7, 10, 12, 15, 17, 19, 21, 23, and 28 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

Claim 7 stands rejected because the specification allegedly does not describe mutants which have twice the incorporation ability of the wild type RNA polymerase. By the present amendment, Claim 7 has been canceled, thereby mooting this rejection. Withdrawal of this rejection is respectfully requested.

Claims 12, 15, 17, 19, 21, and 23 stand rejected as allegedly indefinite in the recitation of "the RNA polymerase of claim..." with additional limitations outside the scope of the claim from which it depends. Without conceding to the merits of this rejection and solely in an effort to expedite prosecution, these claims have been amended as suggested by the Examiner to "An RNA polymerase comprising an RNA polymerase of claim... with a further mutation..." Accordingly, withdrawal of this rejection is respectfully requested.

Claims 10 and 28 stand rejected as allegedly indefinite in that it is unclear whether the additional mutation is limited to the region of the initial incorporation-enhancing mutation. Without conceding to the merits of this rejection, and solely in an effort to expedite prosecution, Claims 10 and 28 have been amended to use the term "comprising" to be consistent with the allowance of a further mutation in the RNA polymerase and to recite that the further substitution, insertion, or deletion is in the "modified wild type RNA polymerase" to clarify that the additional mutation may be anywhere in the sequence of the RNA polymerase rather than confined to the region of the first mutation. In the event that the Examiner deems this language insufficient, Applicants respectfully request that the Examiner contact the Applicants' undersigned representative so that other suitable terminology may be discussed. Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 102

Claims 1, 3, 7-9, and 25 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Sousa *et al.* (*EMBO J.* 14(18):4609-4621 (1995)). Without conceding to the merits of this rejection and solely in an effort to expedite prosecution, Claims 1, 3, 7-9, and 25 have been canceled by the present amendment, thereby mooting the rejection. Accordingly, withdrawal of this rejection is respectfully requested.

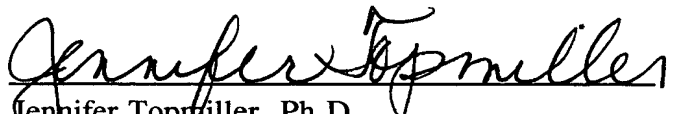
Conclusions

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: 
Jennifer Topmiller, Ph.D.
Registration No. 50,435

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: October 16, 2002

Attachment to REPLY & AMENDMENT dated October 16, 2002

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Paragraph Beginning on Page 8, Line 18, in the

Substitute Specification Filed on May 20, 2002

[Figure 16 (1)-(4)] Figures 16A-16C show an example of sequencing reaction. The reaction was performed by using wild type T7 RNA polymerase (WT) (SEQ ID NOs:17-18)(Figure 16A), mutant T7 RNA polymerase F644Y (F644Y) (SEQ ID NOs:19-20)(Figure 16B), or a mutant T7 RNA polymerase L665P/F667Y (F667Y) (SEQ ID NOs:21-22)(Figure 16C). Sequencing patterns of the same area are shown, and it can be observed that the sequencing could not be correctly performed in the wild type T7 RNA polymerase (WT) (top), because the base call did not correctly function, and interval of bases became too narrow (representations of the bases overlap).

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Paragraph Beginning on Page 9, Line 1, in the

Substitute Specification Filed on May 20, 2002

[Figure 18 (l)-(4)] Figures 18A-18D demonstrate improvement of incorporation rate of dye terminator by mutant T7 RNA polymerase F644Y/L665P/F667Y (SEQ ID NO:23) as an electropherogram.

Attachment to REPLY & AMENDMENT dated October 16, 2002

Marked-up Claims 4, 10, 12, 15, 17, 19, 21, 23, 26, and 28

4. (Three Times Amended) [The RNA polymerase of claim 1,] An RNA polymerase consisting of a wild type RNA polymerase wherein at least one amino acid present in a loop between helix Y and helix Z and/or a loop between helix Z and helix AA in the wild type RNA polymerase has been replaced with tyrosine to enhance the ability of the wild type polymerase to incorporate 3'-deoxyribonucleotides and derivatives thereof in comparison with the corresponding wild type RNA polymerase [of the wild type RNA polymerase is replaced with tyrosine].

10. (Three Times Amended) [The] An RNA polymerase [of claim 1,] comprising a wild type RNA polymerase wherein at least one amino acid present in a loop between helix Y and helix Z and/or a loop between helix Z and helix AA in the wild type RNA polymerase has been modified to enhance the ability of the wild type polymerase to incorporate 3'-deoxyribonucleotides and derivatives thereof in comparison with the corresponding wild type RNA polymerase wherein the modified wild type RNA polymerase has a further substitution, insertion or deletion of an amino acid [other than the modification] in the modified wild type RNA polymerase and wherein the further substitution, insertion, or deletion does not substantially affect the RNA polymerase activity.

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Marked-up Claims 4, 10, 12, 15, 17, 19, 21, 23, 26, and 28

12. (Twice Amended) [The] An RNA polymerase comprising an RNA polymerase of claim 11[, wherein the RNA polymerase from T7 phage has] with a further substitution, insertion, or deletion of an amino acid other than the amino acid residues 644 and/or 667 of SEQ ID NO:2, and wherein the further substitution, insertion, or deletion does not substantially affect the RNA polymerase activity.

15. (Three Times Amended) [The] An RNA polymerase comprising an RNA polymerase of claim 13[,] with a further mutation wherein the 665th amino acid residue, leucine, of SEQ ID NO:2 of the wild type T7 RNA polymerase has been replaced with proline.

17. (Twice Amended) [The] An RNA polymerase comprising an RNA polymerase of claim 16[,] with a further mutation wherein the 665th amino acid residue, leucine, of SEQ ID NO:2 of the wild type T7 RNA polymerase has been replaced with proline.

19. (Twice Amended) [The] An RNA polymerase comprising an RNA polymerase of claim 18[,] with a further mutation wherein the RNA polymerase from T3 phage has a further substitution, insertion, or deletion of amino acid other than the amino

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Marked-up Claims 4, 10, 12, 15, 17, 19, 21, 23, 26, and 28

acid residues 645 and 668 of SEQ ID NO:14, and wherein the further substitution, insertion, or deletion does not substantially affect the RNA polymerase activity.

21. (Twice Amended) [The] An RNA polymerase comprising an RNA polymerase of claim 20[,] with a further mutation wherein the RNA polymerase from K11 phage has a further substitution, insertion, or deletion of amino acid other than the amino acid residues 664-669 and 690 of SEQ ID NO:15, and wherein the further substitution, insertion, or deletion does not substantially affect the RNA polymerase activity.

23. (Twice Amended) [The] An RNA polymerase comprising an RNA polymerase of claim 22[,] with a further mutation wherein the RNA polymerase from SP6 phage has a further substitution, insertion, or deletion of an amino acid other than the amino acid residues 633-638 and 670 of SEQ ID NO:16, and wherein the further substitution, insertion, or deletion does not substantially affect the RNA polymerase activity.

26. (Amended) [The RNA polymerase of claim 9,] An RNA polymerase consisting of a wild type RNA polymerase wherein at least one amino acid present in a region of the wild type RNA polymerase corresponding to amino acid residues 641-667 of SEQ ID NO:2 of RNA polymerase from T7 phage has been replaced with tyrosine to

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Marked-up Claims 4, 10, 12, 15, 17, 19, 21, 23, 26, and 28

enhance the ability of the RNA polymerase to incorporate 3'-deoxyribonucleotides and derivatives thereof into a polynucleotide in comparison with the corresponding wild type RNA polymerase [the amino acid residues 641-667 of SEQ ID NO:2 is replaced with tyrosine].

28. (Amended) [The RNA polymerase of claim 9,] An RNA polymerase comprising a wild type RNA polymerase wherein at least one amino acid present in a region of the wild type RNA polymerase corresponding to amino acid residues 641-667 of SEQ ID NO:2 of RNA polymerase from T7 phage has been modified to enhance the ability of the RNA polymerase to incorporate 3'-deoxyribonucleotides and derivatives thereof into a polynucleotide in comparison with the corresponding wild type RNA polymerase wherein the modified wild type polymerase has a further substitution, insertion, or deletion of an amino acid [other than the modification,] in the modified wild type RNA polymerase which does not substantially affect the RNA polymerase activity.